

(FILE 'HOME' ENTERED AT 19:20:16 ON 16 JAN 2004)

FILE 'REGISTRY' ENTERED AT 19:23:21 ON 16 JAN 2004

L1 STRUCTURE UPLOADED

L2 288 S L1 SSS FUL

FILE 'CAPLUS' ENTERED AT 19:23:57 ON 16 JAN 2004

L3 316 S L2

L4 5 S L3 AND (WOUND OR STRICTURE OR (SKIN (3A) (DAMAGE OR INJUR?)))

L5 1 S WO9606616/PN

L6 1 S L5 AND L3

=> save all

ENTER NAME OR (END):L10070692/1

L# LIST L1-L6 HAS BEEN SAVED AS 'L10070692/L'

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L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:328603 CAPLUS  
 DN 125:1389  
 ED Entered STN: 07 Jun 1996  
 TI Quinazolinone pharmaceuticals for prevention of restenosis  
 IN Nagler, Arnon; Slavin, Shimon; Vlodavsky, Israel; Pines, Mark  
 PA Davidson, Clifford M., USA; Ministry of Agriculture, State of Israel;  
 Hadasit Med. Res. Services and Development Co.  
 SO PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-505  
 CC 1-8 (Pharmacology)  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9606616	A1	19960307	WO 1995-US11186	19950829 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	IL 110831	A1	19981227	IL 1994-110831	19940831
	CA 2198875	AA	19960307	CA 1995-2198875	19950829
	AU 9536268	A1	19960322	AU 1995-36268	19950829
	AU 692307	B2	19980604		
	EP 787000	A1	19970806	EP 1995-933731	19950829
	EP 787000	B1	20001108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1163566	A	19971029	CN 1995-195353	19950829
	CN 1108797	B	20030521		
	JP 10513149	T2	19981215	JP 1995-508990	19950829
	AT 197401	E	20001111	AT 1995-933731	19950829
	US 5891879	A	19990406	US 1996-722046	19961209
PRAI	IL 1994-110831	A	19940831		
	WO 1995-US11186	W	19950829		
OS	MARPAT 125:1389				
AB	The invention provides a pharmaceutical compn. for preventing restenosis by the inhibition of vascular smooth muscle cell (SMC) proliferation, comprising 2-piperidinyl-2-oxopropyl-4(3H)-quinazolinone derivs., preferably halofuginone (I). SMCs isolated from the bovine aortic media were seeded in well culture plates in DMEM in the presence of increasing concns. of I; 80-90% inhibition of SMC proliferation was obtained in the presence of 75 ng I/mL, with an almost complete inhibition at 125 ng/mL.				
ST	piperidinyloxopropylquinazolinone restenosis inhibition; halofuginone vascular smooth muscle proliferation inhibition				
IT	Artery (vascular smooth muscle proliferation inhibition; piperidinyloxopropylquinazolinone for prevention of restenosis)				
IT	Heart, disease (restenosis, piperidinyloxopropylquinazolinone for prevention of restenosis)				
IT	55837-20-2, Halofuginone RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (piperidinyloxopropylquinazolinone for prevention of restenosis)				
IT	55837-20-2, Halofuginone RL: BAC (Biological activity or effector, except adverse); BSU (Biological				

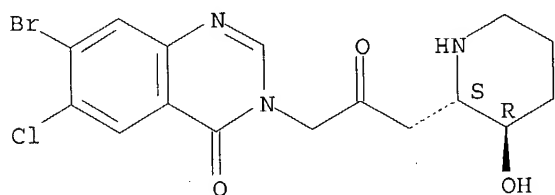
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(piperidinyloxopropylquinazolinone for prevention of restenosis)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidiny]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=>

=> s 12

L3 316 L2

=> s 13 and (wound or stricture or (skin (3a) (damage or injur?)))

L4 5 L3 AND (WOUND OR STRICTURE OR (SKIN (3A) (DAMAGE OR INJUR?)))

=> d 1-5 all, hitstr

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:454111 CAPLUS

DN 139:36533

ED Entered STN: 13 Jun 2003

TI Benzazole derivatives for the treatment of scleroderma

IN Gotteland, Jean-Pierre; Gaillard, Pascale; Chvatchko, Yolande

PA Applied Research Systems ARS Holding N.V., Neth.

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-4184

ICS A61K031-423; A61K031-428; A61K031-506; A61P017-00; A61P009-10;  
A61P011-00; A61P013-12; A61P021-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

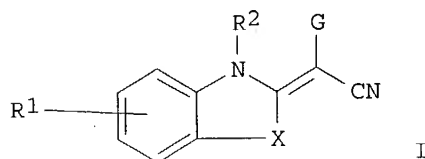
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003047570	A1	20030612	WO 2002-EP13857	20021206
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI EP 2001-727 A 20011207

OS MARPAT 139:36533

GI



AB The present invention is related to the use of benzazole derivs. I [X = O, etc.; G = pyrimidinyl; R1 = H, alkoxy, etc.; R2 = H, alkyl, etc.] for the treatment and/or prevention of scleroderma and its therapeutic implications selected in the group consisting of systemic sclerosis, scleroderma-like disorders, liver cirrhosis, interstitial pulmonary fibrosis, Dupuytren's contracture, keloid and other scarring/wound healing abnormalities, postoperative adhesions, etc. The bioactivities of one compd. of this invention were demonstrated. Formulations are given.

ST benzazole deriv prepn scleroderma treatment

IT Prostaglandins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (I; combination of benzazole deriv. and another therapeutic agent)

IT Nervous system  
 (autonomic, diseases, scleroderma-related; prepn. and effect of  
 benzazole derivs. for treatment of scleroderma)

IT Ion channel blockers  
 (calcium; combination of benzazole deriv. and another therapeutic  
 agent)

IT Nervous system, disease  
 (central, scleroderma-related; prepn. and effect of benzazole derivs.  
 for treatment of scleroderma)

IT Antioxidants  
 (combination of benzazole deriv. and another therapeutic agent)

IT Prostaglandins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (combination of benzazole deriv. and another therapeutic agent)

IT Corticosteroids, biological studies  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (combination of benzazole deriv. and another therapeutic agent)

IT Digestive tract, disease  
 (dysmotility and spasm, scleroderma-related; prepn. and effect of  
 benzazole derivs. for treatment of scleroderma)

IT Heart, disease  
 (failure, chronic; prepn. and effect of benzazole derivs.)

IT Lung, disease  
 (fibrosis, scleroderma-related interstitial pulmonary fibrosis; prepn.  
 and effect of benzazole derivs. for treatment of scleroderma)

IT Heart, disease  
 (infarction; prepn. and effect of benzazole derivs.)

IT Nerve, disease  
 Pain  
 (neuralgia, scleroderma-related trigeminal neuralgia; prepn. and effect  
 of benzazole derivs. for treatment of scleroderma)

IT Anti-inflammatory agents  
 (nonsteroidal; combination of benzazole deriv. and another therapeutic  
 agent)

IT Nerve, disease  
 (peripheral, injury, scleroderma-related; prepn. and effect of  
 benzazole derivs. for treatment of scleroderma)

IT Nervous system, disease  
 (peripheral, scleroderma-related; prepn. and effect of benzazole  
 derivs. for treatment of scleroderma)

IT Surgery  
 (postoperative adhesions; prepn. and effect of benzazole derivs.)

IT Keloid  
 Wound healing  
 (prepn. and effect of benzazole derivs. for treatment of scleroderma)

IT Transport proteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (proton pump inhibitors; combination of benzazole deriv. and another  
 therapeutic agent)

IT Fibrosis  
 (reactive; prepn. and effect of benzazole derivs.)

IT Skin, disease  
 (scar; prepn. and effect of benzazole derivs.)

IT Connective tissue, disease  
 (scleroderma, limited systemic sclerosis; prepn. and effect of  
 benzazole derivs. for treatment of scleroderma)

IT Connective tissue, disease  
 (scleroderma-related Dupuytren's contracture; prepn. and effect of  
 benzazole derivs. for treatment of scleroderma)

IT Cirrhosis

Heart, disease  
Kidney, disease  
(scleroderma-related; prepn. and effect of benzazole derivs. for treatment of scleroderma)

IT Lung, disease  
(scleroderma; prepn. and effect of benzazole derivs. for treatment of scleroderma)

IT Connective tissue, disease  
(scleroderma; prepn. of benzazole derivs. for treatment of scleroderma)

IT Muscle, disease  
(weakness, scleroderma-related; prepn. and effect of benzazole derivs. for treatment of scleroderma)

IT 9002-69-1, Relaxin  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(combination of benzazole deriv. and another therapeutic agent)

IT 60-54-8, Tetracycline 6493-05-6, Pentoxifylline 55837-20-2, Halofuginone 65002-17-7, Bucillamine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination of benzazole deriv. and another therapeutic agent)

IT 9028-06-2 9059-25-0, Lysyl-oxidase 10102-43-9, Nitric oxide, biological studies 11128-99-7, Angiotensin II 39391-18-9, Cyclooxygenase 68651-95-6, Procollagen c-proteinase 123626-67-5, Endothelin-1 135371-29-8, Protein geranylgeranyl transferase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; combination of benzazole deriv. and another therapeutic agent)

IT 82-08-6, Rottlerin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors; combination of benzazole deriv. and another therapeutic agent)

IT 541507-15-7P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of benzazole derivs. for treatment of scleroderma)

IT 99-75-2 110-91-8, Morpholine, reactions 541507-19-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of benzazole derivs. for treatment of scleroderma)

IT 2417-72-3P 68453-56-5P 91271-65-7P 541507-14-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of benzazole derivs. for treatment of scleroderma)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

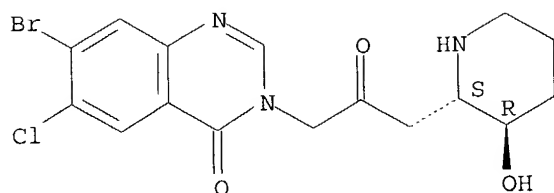
(1) Anon; PATENT ABSTRACTS OF JAPAN 1989, V013(463), PE-833  
(2) Applied Research Systems; EP 1110957 A 2001 CAPLUS  
(3) Hocevar, B; THE EMBO JOURNAL 1999, V18(5), P1345 CAPLUS  
(4) Leroy, E; J CLIN INVEST 1974, V54(4), P880 CAPLUS  
(5) Nec Corp; JP 01180155 A 1989  
(6) Wigley, F; EXPERT OPIN INVESTIG DRUGS 2001, V10(1), P31 CAPLUS

IT 55837-20-2, Halofuginone  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination of benzazole deriv. and another therapeutic agent)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:185574 CAPLUS  
 DN 134:212791  
 ED Entered STN: 16 Mar 2001  
 TI Promotion of **wound** healing with halofuginone  
 IN Pines, Mark; Vlodavsky, Israel; Nagler, Arnon  
 PA Hadasit Medical Research Services and Development Company Ltd., Israel  
 SO PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-505  
 CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017531	A1	20010315	WO 1999-IL441	19990909
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9952995	A1	20010410	AU 1999-52995	19990909
AU 764435	B2	20030821		
EP 1210086	A1	20020605	EP 1999-938491	19990909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508489	T2	20030304	JP 2001-521322	19990909
PRAI WO 1999-IL441	A	19990909		
OS MARPAT 134:212791				
AB	A promoter of <b>wound</b> healing and an inhibitor of formation of a urethral <b>stricture</b> , particularly following surgical intervention or infection in the area is disclosed. Specifically, the most preferred compd. of the present invention, halofuginone, can be used to prevent collagen deposition from occurring within the lumen of the urethra after such trauma, thereby inhibiting urethral <b>stricture</b> formation. Halofuginone, and related compds., are also useful for the promotion of <b>wound</b> healing after trauma, for example after surgery. Efficacy of 1 mg halofuginone/mouse in the promotion of <b>wound</b> healing is shown.			
ST	wound healing promotion halofuginone			
IT	Keloid			
	Wound healing promoters			
	(promotion of <b>wound</b> healing with halofuginone)			
IT	Collagens, biological studies			
	RL: BSU (Biological study, unclassified); BIOL (Biological study)			
	(promotion of <b>wound</b> healing with halofuginone)			
IT	Urethra			
	(strictures of; promotion of <b>wound</b> healing with			

halofuginone)

IT Collagens, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (type III; promotion of **wound** healing with halofuginone)

IT 55837-20-2, Halofuginone  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (promotion of **wound** healing with halofuginone)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

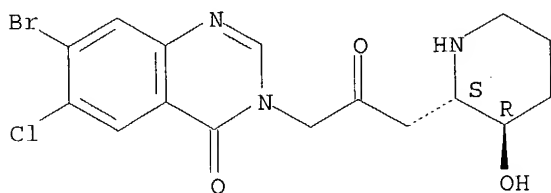
RE  
 (1) Nagler; US 5891879 A 1999 CAPLUS

IT 55837-20-2, Halofuginone  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (promotion of **wound** healing with halofuginone)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:774204 CAPLUS

DN 134:290157

ED Entered STN: 05 Nov 2000

TI The effects of halofuginone, an inhibitor of collagen type I synthesis, on urethral **stricture** formation: in vivo and in vitro study in a rat model

AU Nagler, Arnon; Gofrit, Ofer; Ohana, Meir; Pode, Dov; Genina, Olga; Pines, Mark

CS Department of Bone Marrow Transplantation and Urology, Hadassah University Hospital, Jerusalem, Israel

SO Journal of Urology (Baltimore) (2000) 164(5), 1776-1780

CODEN: JOURAA; ISSN: 0022-5347

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1-8 (Pharmacology)

AB Urethral **strictures** are narrowing of the urethra caused by fibrosis due to excessive collagen prodn. in response to an insult. The effects of halofuginone, a potent inhibitor of collagen .alpha.1(I) gene expression, were evaluated on exptl. induced urethral **strictures** in vivo and on rat urethral fibroblasts in vitro. Applying a coagulation current to the male rat urethra produced urethral **strictures**. Halofuginone was given to the animals for 7 days, starting on the day of **stricture** formation, either orally at 1 and 5 ppm in the diet or by injection of 0.03% halofuginone soln. into the urethra. All the rats were sacrificed on day 21. The coagulation current produced reproducible **strictures** with a typical urethrogram appearance, which were assocd. with increases in collagen .alpha.1(I) gene expression and collagen content at the **stricture** site. Halofuginone injected into the urethra or given orally at 5 ppm normalized the urethrogram and



prevented increases in collagen .alpha.1(I) gene expression and collagen content. Halofuginone at 10-8M inhibited the collagen secretion by fibroblasts derived from the rat male urethra, due to inhibition of the collagen .alpha.1(I) gene expression. Thus, halofuginone prevented **stricture** formation and may become an important mode of therapy in the prevention of restenosis during urethral **stricture** formation.

ST urethra **stricture** halofuginone collagen formation gene

IT Gene, animal

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(collagen .alpha.1(I); halofuginone, an inhibitor of collagen type I synthesis, effect on urethral **stricture** formation)

IT Urethra

(halofuginone, an inhibitor of collagen type I synthesis, effect on urethral **stricture** formation)

IT Collagens, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(type I; halofuginone, an inhibitor of collagen type I synthesis, effect on urethral **stricture** formation)

IT 55837-20-2, Halofuginone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(halofuginone, an inhibitor of collagen type I synthesis, effect on urethral **stricture** formation)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Baskin, L; J Urol 1993, V150, P642 MEDLINE
- (2) Beauboeuf, A; Tissue Cell 1998, V30, P531 MEDLINE
- (3) Chancellor, M; J Urol 1997, V157, P371 MEDLINE
- (4) Halevy, O; Biochem Pharmacol 1996, V52, P1057 CAPLUS
- (5) Holm-Nielsen, A; Br J Urol 1984, V56, P308 MEDLINE
- (6) Levi-Schaffer, F; J Invest Dermatol 1996, V106, P84 CAPLUS
- (7) Nagler, A; Am J Respir Crit Care Med 1996, V154, P1082 MEDLINE
- (8) Nagler, A; Ann Surg 1998, V227, P575 MEDLINE
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- (10) Nyska, M; Connect Tissue Res 1996, V34, P97 CAPLUS
- (11) Peacock, E; Am J Surg 1978, V136, P600 MEDLINE
- (12) Pines, M; Gen Pharmacol 1997, V30, P445
- (13) Pines, M; J Hepatol 1997, V27, P391 CAPLUS
- (14) Scott, T; Urol Int 1980, V35, P334 MEDLINE
- (15) Singh, M; Br J Urol 1975, V47, P871 MEDLINE
- (16) Stormont, T; J Urol 1993, V150, P1725 MEDLINE
- (17) Vandersteen, D; J Urol 1998, V160, P1131 MEDLINE
- (18) Wadhwa, S; J Urol 1998, V159, P1898 MEDLINE
- (19) Webster, G; J Urol 1985, V134, P892 MEDLINE

IT 55837-20-2, Halofuginone

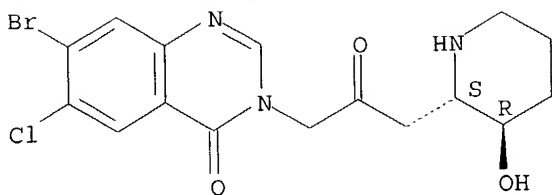
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(halofuginone, an inhibitor of collagen type I synthesis, effect on urethral **stricture** formation)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2000:44827 CAPLUS  
 DN 132:329499  
 ED Entered STN: 19 Jan 2000  
 TI Inhibition of neovascularization and tumor growth, and facilitation of wound repair, by halofuginone, an inhibitor of collagen type I synthesis  
 AU Abramovitch, Rinat; Dafni, Hagit; Neeman, Michal; Nagler, Arnon; Pines, Mark  
 CS Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, 76100, Israel  
 SO Neoplasia (New York) (1999), 1(4), 321-329  
 CODEN: NEOPFL; ISSN: 1522-8002  
 PB Stockton Press  
 DT Journal  
 LA English  
 CC 1-6 (Pharmacology)  
 Section cross-reference(s): 14  
 AB Halofuginone, an inhibitor of collagen .alpha.1(I) gene expression was used for the treatment of s.c. implanted C6 glioma tumors. Halofuginone had no effect on the growth of C6 glioma spheroids in vitro, and these spheroids showed no collagen .alpha.1(I) expression and no collagen synthesis. However, a significant attenuation of tumor growth was obsd. in vivo, for spheroids implanted in CD-1 nude mice which were treated by oral or i.p. (4 .mu.g every 48 h) administration of halofuginone. In these mice, treatment was assocd. with a dose-dependent redn. in collagen .alpha.1(I) expression and dose- and time-dependent inhibition of angiogenesis, as measured by MRI. Moreover, halofuginone treatment was assocd. with improved re-epithelialization of the chronic wounds that are assocd. with this exptl. model. Oral administration of halofuginone was effective also in intervention in tumor growth, and here, too, the treatment was assocd. with reduced angiogenic activity and vessel regression. These results demonstrate the important role of collagen type I in tumor angiogenesis and tumor growth and implicate its role in chronic wounds. Inhibition of the expression of collagen type I provides an attractive new target for cancer therapy.  
 ST halofuginone collagen tumor angiogenesis growth wound  
 IT Neuroglia  
 Neuroglia  
 (glioma, inhibitors; inhibition of neovascularization and tumor growth; and facilitation of wound repair by halofuginone, inhibitor of collagen type I synthesis)  
 IT Antitumor agents  
 (glioma; inhibition of neovascularization and tumor growth, and facilitation of wound repair by halofuginone, inhibitor of collagen type I synthesis)  
 IT Angiogenesis inhibitors  
 Wound healing promoters  
 (inhibition of neovascularization and tumor growth, and facilitation of wound repair by halofuginone, inhibitor of collagen type I synthesis)  
 IT Angiogenesis  
 (neovascularization; inhibition of neovascularization and tumor growth, and facilitation of wound repair by halofuginone, inhibitor

of collagen type I synthesis)  
 IT Collagens, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (type I; inhibition of neovascularization and tumor growth, and facilitation of **wound** repair by halofuginone, inhibitor of collagen type I synthesis)  
 IT 55837-20-2, Halofuginone  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibition of neovascularization and tumor growth, and facilitation of **wound** repair by halofuginone, inhibitor of collagen type I synthesis)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE

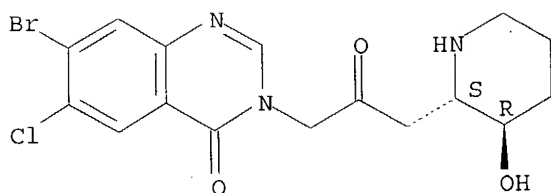
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IT 55837-20-2, Halofuginone  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibition of neovascularization and tumor growth, and facilitation of **wound** repair by halofuginone, inhibitor of collagen type I synthesis)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:548536 CAPLUS  
 DN 129:170522  
 ED Entered STN: 28 Aug 1998  
 TI Treatment and prevention of adhesions  
 IN Pines, Mark; Nagler, Arnon  
 PA Agricultural Research Organization, Ministry of Agriculture, Israel;  
 Hadasit Medical Research Services and Development  
 SO PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-52  
 CC 1-7 (Pharmacology)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834617	A1	19980813	WO 1998-IL69	19980211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5852024	A	19981222	US 1997-797701	19970211
AU 9858776	A1	19980826	AU 1998-58776	19980211
AU 737312	B2	20010816		
EP 996448	A1	20000503	EP 1998-902169	19980211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001511176	T2	20010807	JP 1998-534076	19980211
US 37828	E	20020903	US 2000-733281	20001208
PRAI US 1997-797701	A	19970211		
WO 1998-IL69	W	19980211		

OS MARPAT 129:170522

AB An inhibitor of adhesion formation which can be used to prevent adhesions within the abdominal cavity, particularly following surgical intervention in the area. Specifically, the most preferred compd. of the present invention, Halofuginone, can be used to prevent collagen deposition from occurring within the peritoneum after such surgical intervention, thereby inhibiting adhesion formation. Halofuginone, and related compds., are useful in the prevention and treatment of both inflammatory and surgically induced adhesions, and in the treatment of congenital adhesions. Examples are given for involvement of collagen in adhesion formation, effect of halofuginone on collagen gene expression and content and halofuginone effect on adhesion no.

ST halofuginone adhesion prevention; inflammation inhibitor halofuginone

IT Reproductive tract  
 (adnexitis; halofuginone for adhesion prevention and treatment of inflammation)

IT Adhesion, biological  
 Anti-inflammatory agents

Antibiotics

Wound healing promoters

(halofuginone for adhesion prevention and treatment of inflammation)

IT Collagens, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(halofuginone for adhesion prevention and treatment of inflammation)

IT 55837-20-2, Halofuginone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(halofuginone for adhesion prevention and treatment of inflammation)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 55837-20-2, Halofuginone

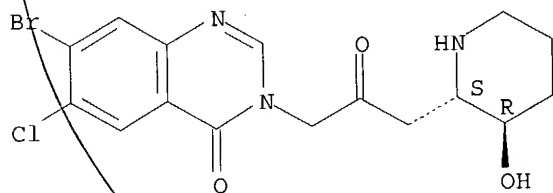
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(halofuginone for adhesion prevention and treatment of inflammation)

RN 55837-20-2 CAPLUS

CN 4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=> s wo9606616/pn